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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/648,790	08/28/2000	James L. Hartley	0942.285000C/RWE/BJD	9852

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EXAMINER
SANDALS, WILLIAM O

ART UNIT	PAPER NUMBER
1636	14

DATE MAILED: 07/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File Cy

Office Action Summary	Application No. 09/648,790	Applicant(s) Hartley et al.
	Examiner William Sandals	Art Unit 1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- *Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.*
- *If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.*
- *If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.*
- *Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).*
- *Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).*

Status

1) ☒ Responsive to communication(s) filed on *Apr 21, 2003*

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *52-69* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideratio

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *52-69* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examine

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Claims

1. Claims 52-69 are pending. Claims 68 and 69 are newly added by amendment in Paper No. 13, filed April 21, 2003.

2. The rejection of claims 52-67 under 35 U.S.C. 112, second paragraph, has been overcome by amendment and the rejection is withdrawn.

3. Claims 52-67 (and newly added claims 68 and 69) stand rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,851,808 (Elledge et al., of record).

Response to Arguments

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 52-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,851,808 (Elledge et al., of record).

The claims are drawn to an in vitro method of cloning a polymerase chain reaction product comprising obtaining a polymerase chain reaction product comprising a first recombination site and a second recombination site which do not recombine with each other and combining the polymerase chain reaction product with a vector comprising a third recombination site and a fourth recombination site which do not recombine with each other under conditions such that recombination occurs between the first and third recombination sites and the second and fourth recombination sites thereby making a product vector. The product vector may be inserted into a host cell. The vector may be an expression vector. The vector may contain a selectable marker, a cloning site, a restriction site, an operon, an origin of replication and a gene or a partial gene. The polymerase chain reaction product may be linear. The recombination sites may be *lox* sites, which may be *loxP* or *loxP511*, or *att* sites, or FRT sites. The recombination protein may be Cre.

Elledge et al. teach at columns 17, 18 and 23-26 an *in vitro* method of recombination between a linear DNA and a host vector using a recombinase enzyme to recombine the linear DNA and a host vector to form a product vector. At columns 29-30 Elledge et al. teach the use of a polymerase chain reaction product comprising obtaining a polymerase chain reaction product comprising a first recombination site and a second recombination site which do not recombine with each other and combining the polymerase chain reaction product with a vector comprising a third recombination site and a fourth recombination site which do not recombine with each other under conditions such that recombination occurs between the first and third recombination sites

and the second and fourth recombination sites thereby making a product vector. This recombination reaction is performed *in vivo*. The product vector may be inserted into a host cell. The vector may be an expression vector. The vector may contain a selectable marker, a cloning site, a restriction site, an operon, an origin of replication and a gene or a partial gene. The polymerase chain reaction product is linear. The recombination sites may be *lox* sites, which may be *loxP* or *loxP511*, or *att* sites, or FRT sites. The recombination protein may be Cre.

Elledge et al. do not teach that the recombination of an amplified nucleic acid and a vector is performed *in vitro*, nor that *att* sites may be *attB* sites, *attP* sites, *atttL* sites or *attR* sites, nor that the recombination *att* recombination proteins are Int Xis or IHF. However, it is well known in the art that *att* sites may be *attB* sites, *attP* sites, *atttL* sites or *attR* sites, and that the *att* recombination proteins are Int, Xis or IHF as taught in Elledge et al. at column 16.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to recombine a linear DNA made by polymerase chain reaction with a vector, where the linear DNA contains two recombination sites which do not recombine with each other, and the vector also contains two recombination sites which do not recombine with each other, and producing a recombinant product DNA as taught by Elledge et al. Elledge et al. teach that a method is being taught for the rapid subcloning of nucleic acid sequences *in vivo* or *in vitro* without the need for restriction enzymes. Elledge et al. make it clear that *in vitro* is an equivalent to the *in vivo* method, thereby making the *in vitro* method an obvious and desirable method for the practice of subcloning by one of ordinary skill in the art. Further, a person of

ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of Elledge et al. who demonstrate the equivalence of *in vitro* and *in vivo* methods of recombination cloning.

Response to Arguments

6. Arguments set forth in Paper No. 13 at page 9, assert that "Elledge et al. does not disclose or suggest a method which comprises two recombination sites on each vector which do not recombine with each other."

As set forth in the rejection above, Elledge et al. teach a method which comprises two recombination sites on a vector and on an amplified DNA which do not recombine with each other, as recited in instant claim 52. Therefore the argument is not found convincing.

7. Arguments set forth in Paper No. 13 pages 9-10, assert that there is no motivation to combine Elledge et al. with Auerbach.

The rejection above does not recite any teachings from Auerbach. Therefore, the arguments are moot.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR

1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Certain papers related to this application are ***welcomed*** to be submitted to Art Unit 1636 by facsimile transmission. The FAX numbers are (703) 308-4242 and 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by the applicant or applicant's representative, and the FAX receipt from your FAX machine is proof of delivery. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications should be directed to Dr. William Sandals whose telephone number is (703) 305-1982. The examiner normally can be reached Monday through Thursday from 8:30 AM to 7:00 PM, EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached at (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to the Tech Center customer service center at telephone number (703) 308-0198.

William Sandals, Ph.D.
Examiner
June 20, 2003

REMY YUCEL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600